

<sup>40</sup>  
~~39~~. (New) The method of claim 37, wherein the immunostimulatory CpG oligonucleotide and the immunopotentiating cytokine are injected directly into the tumor.

<sup>41</sup>  
40. (New) The method of claim 37, wherein the subject is a non-human animal.

<sup>42</sup>  
41. (New) The method of claim 40, wherein the non-human animal is a vertebrate animal selected from the group consisting of a dog, a cat, a horse, a cow, a pig, a sheep, a goat, a chicken, and a primate.

<sup>43</sup>  
~~42~~. (New) The method of claim 41, wherein the tumor is selected from the group consisting of lymphoma and a tumor of the brain, lung, ovary, breast, prostate, colon, and skin.


Remarks:

Applicants have amended the specification to add SEQ ID NOs: to each sequence and to delete a sequence which was inadvertently repeated.

Prior to calculating the fees, please cancel claims 1-20 and add new claims 21-42. Support for new claims 21-42 can be found in originally filed claims 1-20 and in the specification on page 11, lines 19-23 (support that a cytokine is a peptide); page 11, lines 17-27 (support for recited cytokines); page 30, lines 3-31 (support for unmethylated status of the C residue in a CpG dinucleotide); the Examples (support for the CpG oligonucleotide and the antigen not being conjugated to each other); and page 9-11 and 44 (support for lymphoma).

No new matter has been added.

Respectfully submitted,

  
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Attorney Docket No: C1039/7049 (ERG/HCL)  
April 2, 2001  
Xndd

MARKED-UP SPECIFICATION

Please insert the following paragraph on page 1, in the first line after the title as follows:

This application is a divisional of U.S. Patent Application Serial Number 09/286,098, filed April 2, 1999, pending, which claims priority under 35 U.S.C. §119(e) from U.S. Provisional Application Serial Number 60/080,729 (now abandoned) filed April 3, 1998. The entire contents of all the foregoing patent applications are incorporated by reference herein.

Please re-write the paragraph starting on page 16, line 13, as follows:

As described in co-pending patent application US Serial No. 08/960,774, oligonucleotides containing an unmethylated CpG motif (i.e. TCCATGACGTTCTGACGTT; SEQ IN NO: [93] 100), but not a control oligonucleotide (TCCATGAGCTTCCTGAGTCT; SEQ ID NO: 103) prevented the development of an inflammatory cellular infiltrate and eosinophilia in a murine model of asthma. Furthermore, the suppression of eosinophilic inflammation was associated with a suppression of Th2 response and induction of a Th1 response.

Please re-write the paragraph starting on page 33, line 26, as follows:

The nucleic acid sequences of the invention which are useful for inducing immune remodeling are those broadly described above and disclosed in PCT Published Patent Applications claiming priority to U.S. Serial Nos. 08/738,652 and 08/960,774, filed on October 30, 1996 and October 30, 1997 respectively. Exemplary sequences include but are not limited to those immunostimulatory sequences shown in Table 1 as well as

TCCATGTCGCTCCTGATGCT (SEQ ID NO: 47), TCCATGTCGTTCTGATGCT (SEQ ID NO: 48), TCGTCGTTTTGTCGTTTTGTCGTT (SEQ ID NO: [53] 90), TCGTCGTTGTCGTTGTCGTT (SEQ ID NO: 89); [TCGTCGTTTTGTCGTTTTGTCGTT (SEQ ID NO: 90),] TCGTCGTTGTCGTTTTGTCGTT (SEQ ID NO: 91), GCGTGCGTTGTCGTTGTCGTT (SEQ ID NO: 92), TGTCGTTTGTCGTTTGTCGTT (SEQ ID NO: 94), TGTCGTTGTCGTTGTCGTT (SEQ ID NO: 96) TCGTCGTCGTCGTT (SEQ ID NO: 97), TCCTGTCGTTCTTGTCGTT (SEQ ID NO: 79), TCCTGTCGTTTTTTGTCGTT (SEQ ID NO: 81), TCGTCGCTGTCTGCCCTTCTT (SEQ ID NO: 82), TCGTCGCTGTTGTCGTTTCTT (SEQ ID NO: 83), [TCGTCGTTTTGTCGTTTTGTCGTT (SEQ ID NO: 90), TCGTCGTTGTCGTTTTGTCGTT (SEQ ID NO: 91)

TGTCGTTGTCGTTGTCGTT (SEQ ID NO:96),] TCCATGACGTTTCCTGACGTT (SEQ ID NO:100), GTCG(T/C)T (SEQ ID NO:101) and TGTCG(T/C)T (SEQ ID NO:102).

Please re-write the paragraph starting on page 45, line 8, as follows:

Immunization: Two phosphorothioate CpG oligonucleotides were purchased commercially and produced under GMP conditions (Oligos Etc., Wilsonville, OR). Both oligonucleotide sequences had similar effects in all assays. CpG oligonucleotide 1758 was used unless stated otherwise. Oligonucleotide 1758 had the sequence

TCTCCCAGCGTGCGCCAT (SEQ ID NO:104)

and oligonucleotide 1826 had the sequence

TCCATGACGTTTCCTGACGTT (SEQ ID NO:[3] 105)

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MARKED-UP CLAIMS:

Please cancel claims 1-20.

Please add new claims 21-42 as follows:

21. (New) A method for stimulating an immune response in a subject, comprising:  
administering to a subject exposed to an antigen an effective amount for inducing a synergistic antigen specific immune response of an immunopotentiating cytokine selected from the group consisting of IL-3, IL-5 and IL-12, and an immunostimulatory CpG oligonucleotide having a sequence including at least the following formula:



wherein the oligonucleotide includes at least 8 nucleotides wherein C is unmethylated and wherein  $X_1$  and  $X_2$  are nucleotides, wherein the cytokine is a peptide, whereby an antigen is optionally additionally administered, and wherein the antigen and the CpG oligonucleotide are not conjugated.

22. (New) The method of claim 21, wherein the immunopotentiating cytokine is an antigen-cytokine fusion protein.

23. (New) The method of claim 21, wherein the antigen is selected from the group consisting of a tumor antigen, a microbial antigen, and an allergen.

24. (New) The method of claim 23, wherein the antigen is a tumor antigen.

25. (New) The method of claim 21, wherein the antigen is administered to the subject in conjunction with the immunostimulatory CpG oligonucleotide and the immunopotentiating cytokine.

26. (New) The method of claim 21, wherein the subject is passively exposed to the antigen.

27. (New) The method of claim 21, wherein the subject has a neoplastic disorder.

28. (New) The method of claim 21, wherein the subject has a viral infection.

30. (New) The method of claim 21, wherein the subject is a non-human animal.

30. (New) The method of claim 29, wherein the non-human animal is a vertebrate animal selected from the group consisting of a dog, a cat, a horse, a cow, a pig, a sheep, a goat, a chicken, and a primate.

31. (New) A composition, comprising:  
an effective amount for synergistically activating a dendritic cell of an immunostimulatory CpG oligonucleotide having a sequence including at least the following formula:



wherein the oligonucleotide includes at least 8 nucleotides wherein C is unmethylated and wherein  $X_1$  and  $X_2$  are nucleotides; and a cytokine selected from the group consisting of IL-3, IL-5 and IL-12, wherein the cytokine is a peptide.

32. (New) The composition of claim 31, wherein the cytokine is IL-3.

33. (New) The composition of claim 31, further comprising an antigen and wherein the antigen and the CpG oligonucleotide are not conjugated.

34. (New) The composition of claim 33, wherein the antigen is selected from the group consisting of a cancer antigen, a microbial antigen, and an allergen.

35. (New) A method for activating a dendritic cell, comprising:  
contacting a dendritic cell exposed to an antigen with an effective amount for synergistically activating a dendritic cell of an immunopotentiating cytokine selected from the group consisting of IL-3, IL-5 and IL-12, and an immunostimulatory CpG oligonucleotide having a sequence including at least the following formula:



wherein the oligonucleotide includes at least 8 nucleotides wherein C is unmethylated and wherein  $X_1$  and  $X_2$  are nucleotides, wherein the cytokine is a peptide, whereby an antigen is optionally additionally administered, and wherein the antigen and the CpG oligonucleotide are not conjugated.

36. (New) The method of claim 35, wherein the antigen is a tumor antigen.

37. (New) A method for treating a subject having a neoplastic disorder, comprising:

administering to the tumor of a subject having a neoplastic disorder an immunopotentiating cytokine selected from the group consisting of IL-3, IL-5 and IL-12, and an immunostimulatory CpG oligonucleotide having a sequence including at least the following formula:



wherein the oligonucleotide includes at least 8 nucleotides wherein C is unmethylated and wherein  $X_1$  and  $X_2$  are nucleotides, in an amount effective for synergistically increasing survival time of the subject with respect to a subject administered the immunostimulatory CpG oligonucleotide or the immunopotentiating cytokine alone, wherein the cytokine is a peptide.

38. (New) The method of claim 37, wherein the tumor is selected from the group consisting of a lymphoma and a tumor of the brain, lung, ovary, breast, prostate, colon, and skin.

39. (New) The method of claim 37, wherein the immunostimulatory CpG oligonucleotide and the immunopotentiating cytokine are injected directly into the tumor.

40. (New) The method of claim 37, wherein the subject is a non-human animal.

41. (New) The method of claim 40, wherein the non-human animal is a vertebrate animal selected from the group consisting of a dog, a cat, a horse, a cow, a pig, a sheep, a goat, a chicken, and a primate.

42. (New) The method of claim 41, wherein the tumor is selected from the group consisting of lymphoma and a tumor of the brain, lung, ovary, breast, prostate, colon, and skin.